

The claims are 1-21. Claims 22-39 have been canceled as being directed to unelected subject matter without prejudice to Applicants' pursuit of the subject matter in any other application.. Claims 1-14 are under consideration. Claims 15-21, drawn to methods of use of compounds of claims 1-14 are being maintained to allow rejoinder should the claims in Group I be found allowable.

### **Remarks**

#### **I. Rejections under 35 USC 112:**

Claims 11-13 are rejected as allegedly not described to enable one skilled in the art to make and/or use the invention. Applicants respectfully traverse the rejection.

Claims 11-13 are directed to compositions comprising a compound according to claim 1, or a pharmaceutically acceptable salt or N-oxide thereof; and

- i) an anti-neoplastic, anti-tumor, anti-angiogenic, or chemotherapeutic agent
- ii) a cytotoxic cancer therapeutic agent, or
- iii) an angiogenesis inhibiting cancer therapeutic agent.

Applicants respectfully submit that compositions that include such agents are well known in the industry and thus the recited description is sufficient to enable one in the art to make and/or use the invention. Claims 11-13 are composed of two elements: the compound of claim 1, and the anti-neoplastic, anti-tumor, anti-angiogenic agent, or chemotherapeutic, cytotoxic cancer therapeutic agent, or angiogenesis inhibiting cancer therapeutic agent. The compound according to claim 1 is described in the specification sufficient to enable one in the art to make and/or use the compound. Further, the terms anti-neoplastic, anti-tumor, anti-angiogenic agent, or chemotherapeutic, cytotoxic cancer therapeutic agent, or angiogenesis inhibiting cancer therapeutic agent are well known to one in the art.

MPEP 2164.01 describes the test of enablement as whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. Thus, the compositions comprising the mixture of a compound with an anti-neoplastic, anti-tumor, anti-angiogenic agent, or chemotherapeutic, cytotoxic cancer therapeutic agent, or

angiogenesis inhibiting cancer therapeutic agent are well within the common knowledge of one in the art – sufficient to enable the practitioner to make and/or use the invention without undue experimentation. In fact, one in the art with hardly any experimentation at all can make the compositions.

Applicants respectfully point out that the *Wands* factors are listed under MPEP 2164.01(a) “Undue Experimentation Factors”, that is, factors used in the inquiry as to how much experimentation is “undue.” MPEP 2164.01(b) points out that as long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement is satisfied. Applicants respectfully cite paragraph 85 which states that the compositions of the invention or compositions used by the methods of the invention comprise a compound of the invention and optionally other therapeutic ingredients or adjuvants. Paragraphs 86 to 102 describe various methods of making and using such compositions, including dosages of the compounds of the invention. Paragraphs 103 and 104 describe the additional agents that can be part of the compositions described previously. Accordingly, the specification discloses many methods for making and using the compositions claimed in claims 11-13 and the claims are described sufficiently to enable one in the art to make and/or use the invention.

The Examiner has stated that there is no working example in the specification. Applicants respectfully disagree. There are nineteen working examples of compounds of the invention. The rejected claims are merely mixtures of the compounds of the invention and agents readily determined and known by one in the art. Thus, the nature of the claims is a composition that is highly predictable and easy to make. Nonetheless, the specification provides ample direction on how to make such compositions. Thus, the specification describes the claimed invention sufficiently to enable one in the art to make and/or use the invention. Applicants respectfully submit that the rejection has been overcome and request withdrawal of the rejection.

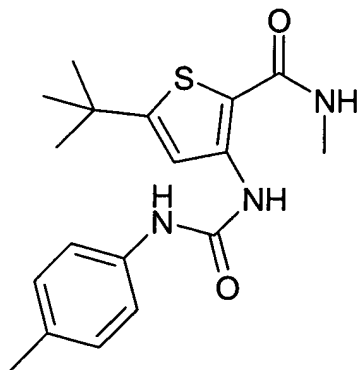
## **II. Rejections Under 35 USC 103**

Claims 1-14 have been rejected as allegedly obvious in view of U.S. Patent No. 6,187,799 (“Wood”). Applicants respectfully traverse the rejection.

Independent claims 1 and 14 disclose thiophene ring compounds having two features as described in Formula (I) of Claim 1: i) an amido linkage attached by the carboxy carbon to a site adjacent to the ring sulfur atom, wherein that amido is substituted by R1; and ii) adjacent to that amido site is an methyl amine substituted by R2. To make a *prima facie* case of obviousness, a reference (or combination of references) must include all the elements of a claim. Applicants respectfully submit that Wood alone or in combination with the compound CAS RN 216574-52-6 does not disclose any thiophene compounds having the two elements described in claim 1 or exemplified by the compounds of claim 14 of the present invention. Applicants respectfully submit that a *prima facie* case has not been made by the Examiner of obviousness and request withdrawal of the rejection.

Further, if for arguments sake a *prima facie* case were made, the claims are nevertheless not obvious in light of Wood alone or in combination with the compound CAS RN 216574-52-6 because there is no motivation, teaching, or suggestion of compounds of the present invention. Indeed, Wood teaches away from the compounds of the present invention.

Wood discloses thirty compounds (col. 1, line 52 to col. 7, line 10; and set forth as Examples 1-30). Of the thirty Wood compounds, only one – Example 4, col. 2, lines 35-50 – discloses a thiophene ring with an amido linkage attached by the carboxy carbon to a site adjacent to the ring sulfur atom. That compound is described as 5-tert-butyl-3-(3-p-tolyl-ureido)-thiophene-2-carboxylic acid methylamide:



None of the other remaining twenty-nine compounds in Wood have an amide attached by the carboxy carbon to a position adjacent to a thiophene sulfur ring atom – one feature of the compounds claimed in independent Claim 1 of the present application.

Of the remaining twenty nine Wood compounds, five have an alkyl and a ureido at the two positions adjacent to a thiophene sulfur ring atom; twenty have an alkyl and an ester at the two positions adjacent to a thiophene sulfur ring atom; two have an alkyl and an ester at the two positions adjacent to a furan oxygen ring atom; and two have an alkyl and an ester at the two positions adjacent to a pyrrole ring nitrogen atom.

Wood discloses at col. 7, line 17 to col. 8, line 54 that twelve of the thirty Wood compounds are preferred. The Wood Example 4 is not among the preferred twelve compounds. Further, Wood discloses at col. 8, line 55 to col. 9, line 47 that six compounds are more preferred. The Wood Example 4 is not among the more preferred six compounds.

Each of the more preferred Wood thiophene compounds have adjacent to the ring sulfur atom i) an alkyl moiety and ii) either an alkyl ester or a ureido moiety. One reading Wood is taught that the sole compound (Wood Example 4) having an amide attached by the carboxy carbon to a position adjacent to a thiophene sulfur ring atom is not preferred nor more preferred. Thus, one reading Wood is taught away from that compound (Example 4) and the compounds of the present invention.

The CAS RN 216574-52-6 compound does not add any teaching, motivation or suggestion of the present invention. Thus, one reading Wood alone or in combination with the compound CAS RN 216574-52-6 is simply given no teaching, motivation, or

suggestion to modify the Wood Example 4 or CAS RN 216574-562-6 to expect any success and produce the compounds of the present invention.

Applicants respectfully submit that the rejection has been traversed and independent claims 1 and 14 are not obvious in light of Wood alone or in combination with the compound CAS RN 216574-52-6. Claims 2-13, dependent on independent claim 1, are also not obvious in light of Wood alone or in combination with the compound CAS RN 216574-52-6 for that reason as well as for the additional limitations recited by them. Accordingly, Applicants respectfully submit that the rejection has been overcome and request its withdrawal.

### **III. Conclusion**

Applicants respectfully submit that the rejections have been overcome and request their withdrawal. Further, Applicants respectfully suggest that claims 1-14 are allowable and request rejoinder of claims 15-21 directed to methods of use of the novel and unobvious compounds of claims 1-14.

Applicants believe that no fee is needed. Nevertheless, the Examiner is authorized to charge any deficiencies in fees and credit any overpayment to OSI Pharmaceuticals, Inc. Deposit Account No. **50-2783**.

Attorney for Applicants can be reached at the telephone number and address below.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date appearing below.

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